REMARKS

The present application was originally filed with Claims 1-24 which were subject to a restriction requirement. Claims 1-3, 5, 6, 13-15, 17 and 18 drawn to recombinant DNA molecules and expression vectors, host cells and diagnostic tests using the nucleic acids were elected. New Claims 25 through 35, which fall within the elected group, have been added by the present amendment. The present amendment cancels original Claims 4, 7-12, 16, 19, 20 and 21-24, without prejudice, as being drawn to non-elected inventions. Thus, Claims 1-3, 5, 6, 13-15, 17-18 and 25-35 are under active prosecution.

Applicants submit concurrently herewith a Substitute Sequence Listing in computer readable and paper form which fully complies with the requirements of 37 C.F.R. § 1.821- 1.825. Applicants also submit herewith a statement that the Substitute Sequence Listing in computer readable and paper form are the same and do not contain any new matter.

I. The Invention

The present invention generally relates to novel nucleotide sequences that encode novel chemokines of the C-C family, PANEC-1 and PANEC-2, found expressed in pancreatic tissue. The presently claimed invention also relates to expression vectors and host cells comprising nucleic acid encoding PANEC-1 and PANEC-2 and methods for the detection of nucleic acid sequences encoding PANEC-1 and PANEC-2 .

II. Amendments to the Claims and Specification

Claims 1 and 13 have been amended to recite an isolated polynucleotide sequence comprising nucleic acid encoding the polypeptide disclosed in SEQ ID

NO:2. Basis for the amendments to Claims 1 and 13 can be found in the specification at page 9, lines 21-28, which disclose that as a result of the degeneracy of the genetic code, there may be numerous nucleotide sequences encoding PANEC-1 and PANEC-2. Basis for the amendments to Claim 1 and 13 can also be found at page 10, lines 2-8, which disclose that the nucleotide sequences encoding PANEC-1 and PANEC-2 may be altered to give more desirable properties to the proteins, such as, greater half-life or to increased expression in specific expression systems.

New Claims 25 and 26, which depend from Claims 1 and 13, respectively, have been added which recite that the polynucleotides comprise SEQ ID NO: 1 and SEQ ID NO:3, respectively. Basis for new Claims 25 and 26 can be found throughout the specification as filed in particular in the SEQUENCE LISTING and in Figures 1 and 2.

Independent Claims 27, 28, 31 and 32 have been added which relate to diagnostic tests for the detection of nucleic acid sequences encoding PANEC-1 and PANEC-2. Basis for new Claims 27 and 29 can be found at page 8, lines 3-18 and 27-31; page 9, lines 1-20 and the paragraph bridging page 9 and 10; page 10, lines 18-27; page 11, lines 3-8 and 14-22 and page 11, lines 23-31.

Dependent Claims 29 and 30 have been added which recite the diagnostic test wherein the condition associated with inflammation occurs in the pancreas. Basis for these dependent claims can be found at page 5, lines 15-18 and page 8, lines 27-31.

Claim 33 has been added which recites the diagnostic test of Claim 32 wherein said fragment is selected from the nucleic acid sequence encoding amino acid residues 93-128 of Figure 2. Basis for this claim can be found in Figure 3 which is an alignment of related chemokines. Figure 3 demonstrates

that the region encoding amino acid residues 93-128 is non-conserved among chemokine family members and is specific to PANEC-2.

Claims 34 and 35 have been added which recite the amino acid sequence for PANEC-1 and PANEC-2 beginning at specific amino acid residues which represent the N-terminal amino acid residue of mature PANEC-1 and PANEC-2, respectively. Basis for these claims can be found in Figures 1 and 2, which disclose the amino acid sequence for PANEC-1 and PANEC-2, and Figures 4 and 5 which are hydrophobicity plots for PANEC-1 and PANEC-2, respectively. For those of skill in the art, it is understood that cleavage of signal sequences occurs at or near the C-terminal end of a predicted hydrophobic region located at the N-terminus of the full length protein. Therefore, mature PANEC-1 is predicted to have an N-terminal sequence of amino acid residue 24, glycine, and mature PANEC-2 is predicted to have an N-terminal sequence of amino acid residue 21, threonine.

III. Objection to the Drawings

The Examiner has objected to Figures 1 and 3 because they contain sequences that are not indicated in the Sequence Listing. Applicants submit concurrently herewith a Substitute Sequence Listing in computer readable and paper form which fully complies with the requirements of 37 C.F.R. § 1.821-1.825. Applicants have amended the specification, including the "Description of the Figures" to include sequence identifiers for the nucleotide sequences disclosed in Figures 1 and 3, thereby obviating the Examiner's objection.

In view of the amendments to the specification, Applicants respectfully request a withdrawal of the objection to the drawings.

IV. Section 112, 1st Paragraph Objection to the Specification and Rejection of Claims 2-3 and 14-15

The Examiner has objected to the specification and rejected Claims 2-3 and 14-15 under 35 U.S.C. 112, first paragraph. The Examiner states that the specification fails to provide an enabling disclosure for a diagnostic test for activated or inflammatory conditions of the pancreas and specifically for a diagnostic test for pancreatitis, employing panec-1 and panec-2 nucleic acid probes. The Examiner states that the art of chemokines is unpredictable and that there are no analogous compounds in the prior art from which one might draw generic enablement. The Examiner concludes that it would require undue experimentation for one to practice the methods of Claims 2-3 and 14-15.

Applicants respectfully traverse this objection to the specification and rejection of Claims 2-3 and 14-15 under Section 112, first paragraph.

Applicants have canceled Claims 2-3 and 14-15, without prejudice, and have replaced them with Claims 25-32. New independent Claims 27-28 and 31-32 recite a diagnostic test for the detection of nucleic acid sequences encoding the chemokines PANEC-1 and PANEC-2 wherein the presence of the chemokines positively correlates with conditions associated with inflammation, particularly of the pancreas. Applicants respectfully submit that the teachings of the specification, in combination with the knowledge of those of skill in the art at the time of filing of the present application, fully enable a diagnostic test for the detection of nucleic acid sequences encoding PANEC-1 and PANEC-2, wherein the presence of an abnormal level of the novel chemokines is positively correlated with a condition associated with inflammation.

1. Correlation of PANEC-1 and PANEC-2 with Inflammation

The Examiner states at page 6, lines 7-9 of the Office Action:

> ... neither the art nor the specification teaches that the detection of PANEC-1 or PANEC- 2 may be correlated with a disease state ...

Applicants submit that the Examiner has given no reasonable basis whatsoever to doubt that the novel chemokines of the present invention would be involved in conditions related to inflammation, such as disease states. In fact, by definition, chemokines are molecules that function as regulators of inflammatory processes (Schall, The Chemokines, The Cytokine handbook, Academic Press, 1994 September 19-20, Second Edition, pg 4, IDS reference AT) and are involved in various inflammatory responses (Advances in Experimental Medicine and Biology vol. 351 (1993) The Chemokines, edited by Lindley et al Plenum Press, New York, pg. 20).

As noted by the Court of customs and Patent Appeals ("CCPA") in In re Marzocchi, 439 F.2d 220, 169 USPQ 367 (CCPA 1967):

> "... a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken in compliance with the enabling requirement of the first paragraph of § 112 unless there is a reason to doubt the objective truth of the statement contained therein which must be relied on for enabling support." In re Marzocchi, supra.

As further explained in In re Marzocchi, the CCPA noted that even in cases of unpredictable chemical reactions where there may be reason to doubt the accuracy of broad statements of enablement, such cases will usually involve cases "where the statement is, on its face, contrary to generally accepted scientific principles." Id. At 367. Additionally, the court clearly stated in In re Brana, 34 USPQ2d 1436 (Fed. Cir. 1995), that there is a presumption of enablement, which must be overcome by the Patent Office in rejecting an application under Section

112, first paragraph.

Furthermore, Applicants submit that it is the burden of the PTO to provide substantive evidence that one of skill in the art would have reasonably doubted the enablement of the presently claimed invention, which recites a method for the detection of panec-1 and panec-2 nucleic acid sequences, wherein the presence of an abnormal level of the novel chemokines correlates positively with a condition associated with inflammation. The Examiner has provided no substantive evidence whatsoever that the statements of enablement of this application relating to detection methods would have been doubted by one of skill in the art or that those statements are contrary to generally accepted scientific principles.

In contrast, the state of the art as of the effective filing date of the present application supports the opposite conclusion. Applicants submit that for those of skill in the art, it is well known that chemokines function as regulators of inflammatory and immunoregulatory processes through their specific leukocyte chemoattractant effects (Schall supra pg.4), that chemokines are involved in a variety of disease processes possessing an inflammatory component, and that high levels of chemokines are found in inflammatory disease states (Schall supra pg. 49). Furthermore, it is well known by those of skill in the art that other members of the C-C family of chemokines, RANTES, MCP-1, MCP-2, MCP-3, MIP 1-a and MIP 1-ß, with which PANEC-1 and PANEC-2 share significant homology (see page 6, lines 1-3 and Figure 3 of the present specification) induce the migration of monocytes which are involved in the inflammatory process (Schall, pg. 25-27). Additionally, Schall, at page 30, reports that C-C chemokines are potent eosinophil chemoattractants, with the role of eosinophils in inflammatory processes being well documented. Therefore, Applicants contend that one of skill in the art,

following the teachings of the present application would have no reason to doubt that abnormal levels of PANEC-1 and PANEC-2 would be involved in conditions associated with inflammation. Furthermore, Applicants contend that those of skill in the art would have no reason to doubt that abnormally high levels of nucleic acid encoding PANEC-1 and PANEC-2 appearing in pancreatic tissue would be indicative of a condition related to inflammation of the pancreas, as is recited in dependent Claims 29-30.

2. Level and Specificity of Expression of PANEC-1 and 2

The Examiner at page 6, 2nd full paragraph of the present Office Action questions the level and specificity of expression of the novel chemokines PANEC-1 and PANEC-2 with respect to the pancreas. The Examiner states that there is no guidance in the specification to allow one to determine what constitutes an abnormal deviation in levels of PANEC expression and therefore what differences are indicative of pathology.

Applicants submit that the present specification teaches that PANEC-1 and PANEC-2 were found among the cDNAs made from human pancreatic tissue, see page 5, lines 14-18 and page 14, lines 8-11; identifies PANEC-1 and PANEC-2 as C-C chemokines, see page 5, lines 15-18 and 27-31, which are known to be associated with inflammation; and teaches methods of hybridization assays for the detection of nucleic acid sequences encoding PANEC-1 and PANEC-2 at page 8, lines 14-18 and page 9, lines 10-20. Furthermore, the Examiner states at page 6 of the outstanding Office Action that the prior art enables methods of performing hybridization assays using known nucleic acid sequences.

Therefore, Applicants assert that the absolute level and specificity of expression of PANEC-1 and PANEC-2 are irrelevant to Claims 27-28 and 31-32

which recite a diagnostic test for the detection of nucleic acids that involves comparing the amount of nucleic acid sequences detected in a sample with the amount detected in a standard thereby determining abnormal levels. Although nucleic acid encoding the PANEC molecules were found in a cDNA library made from pancreatic tissue, Claims 27-28 and 31-32 do not require a knowledge of the absolute level or specificity of the novel chemokines in a given tissue in order to be enabled. The presence of an abnormal level is determined by comparison with a standard and Applicants contend that the use of standards in hybridization assays is deemed to be routine to those of ordinary skill in the art.

Additionally, Applicants submit that the disclosure of the present specification, which identifies PANEC-1 and PANEC-2 as members of the C-C chemokine family, fully enables a diagnostic test for the detection of nucleic acid sequences encoding PANEC-2 and PANEC-2 wherein the presence of abnormal levels of the nucleic acid sequences correlate with a condition associated with inflammation and specifically, inflammation of the pancreas. Therefore, Applicants submit that new Claims 27-32 fully comply with Section 112, 1st paragraph requirements.

3. Mechanism of Action of Chemokines Not Relevant to Claimed Invention

The Examiner states at page 6 of the outstanding Office Action that while the specification teaches that excessive expression of either PANEC-1 or PANEC-2 can lead to activation of monocytes, macrophages, basophils, eosinophils, T lymphocytes and/or other cells, The Examiner further states at page 7, 1st full paragraph:

"However it is not clear what the basis for the assertion that excessive expression of PANEC-1 and 2 results in the variety of effects taught as no data is presented that PANEC-1 and 2 products actually play a direct role in these processes;"

The Examiner appears to agree that diverse pathologies are associated with changes in the levels of chemokines; that chemokines are linked to complex signal transduction pathways. However, the Examiner concluded that chemokines are unpredictable and lab data are required.

Firstly, Applicants submit that the Examiner has provided no evidence to support her contention that the novel C-C chemokines, PANEC-1 and 2, would function contrary to other known C-C chemokines or that one of skill in the art would doubt that a C-C chemokine would activate monocytes, macrophages, basophils, eosinophils, T lymphocytes and/or other cells. Applicants respectfully point out that the Examiner's interpretation of the claimed invention is not unfettered. As stated by the CCPA in In re Moore and Janoski, 169 USPQ 236 (58 CCPA 1042, 439 F.2d 1232, 1971):

> . . . language employed in claims must be analyzed---not in a vacuum, but always in light of teachings of prior art and of the particular application disclosure as it would be interpreted by one possessing ordinary skill in pertinent art . . . (emphasis added)

Applicants point out that those of skill in the art, given the teachings of the present application, would expect and predict PANEC-1 and PANEC-2 to function similarly to other known C-C chemokines in activating monocytes, macrophages, basophils, eosinophils, T lymphocytes and/or other cells which respond to chemokines by producing abundant proteases and other molecules which can lead to tissue damage or destruction and to be associated with inflammatory conditions.

Additionally, Applicants invite the Examiner's attention to pending

Claims 27-28 and 31-32 which recite methods for the detection of the nucleic acid sequences encoding PANEC-1 and PANEC-2. The detection of PANEC-1 and -2 encoding nucleic acid sequences does not depend on knowledge of the underlying mechanism of action of the novel chemokines in order to be enabled. Applicants contend that one of skill in the art would be able to detect a nucleic acid sequence through standard hybridization conditions regardless of the mechanism by which the translated protein works. Furthermore, the presence of an abnormal level of PANEC-1 and 2 in a biological sample that is correlated with an inflammatory condition does not require demonstration of the mechanism of action of PANEC-1 and PANEC-2.

Rather than being unpredictable, chemokines by definition are predictably associated with inflammatory conditions (see Schall supra; Advances in Experimental Medicine and Biology supra), as is asserted by Applicants in their specification. The Examiner provides no evidence or support to the contrary. Therefore, Applicants contend that Claims 27-32 are in full compliance with Section 112, first paragraph requirements.

4. Generic Enablement

The Examiner states at page 8, lines 2-6 that while the panec-1 and panec-2 sequences (SEQ ID NO:1 and 3) are novel, there are no analogous compounds in the prior art from which one might draw generic enablement for claims which recite a diagnostic assay.

Applicants strongly disagree and respectfully point out to the Examiner that there are numerous, related family members in the art which are both structurally and functionally related to PANEC-1 and PANEC-2. Applicants invite the Examiner's attention to Figure 3 which illustrates an amino acid

alignment of PANEC-1 and PANEC-2 and other human members of the C-C chemokine family, and Figure 6 which illustrates the phylogenetic tree of human C-C chemokines. Figures 3 and 6 demonstrate that members of the C-C chemokine family have a high degree of amino acid sequence and structural relatedness and are in fact, characterized by their structural and functional relatedness (Schall supra). Art contemporaneous with the filing date of the present application illustrates that C-C family members are functionally related. For example, it is recognized that C-C chemokines are chemoattractants for monocytes (Advances in Experimental Medicine and Biology supra, IDS reference AT and MCP-1 has been implicated in mediating monocyte infiltration in a variety of inflammatory disease states (Charo et al 1994 Proc. Natl. Acad. Sci. 91:2752-2756, attached hereto as Exhibit A). Therefore, Applicants submit that the nucleic acid sequences encoding PANEC-1 and PANEC-2 (SEQ ID NO:1 and SEQ ID NO:3, respectively) are novel and encode proteins having structural and functional relatedness to well characterized C-C chemokines which are known by those of skill in the art to be associated with inflammatory conditions. Therefore, Applicants assert that Claims 27-32 are in full compliance with Section 112, first paragraph requirements.

5. Undue Experimentation

The Examiner alleged that it would require undue experimentation to practice the presently claimed diagnostic methods; however, this statement contradicts the Examiner's earlier conclusion at page 6 of the outstanding Office Action that the prior art enables methods of performing hybridization assays using known nucleic acid sequence.

Applicants submit that there is sufficient information provided by the

present application so that one of skill in the art could practice the claimed methods without the need for undue experimentation. The nucleic acid sequences of PANEC-1 and 2 are given in the Figures and Sequence Listing and the present specification teaches methods of hybridization assays for the detection of nucleic acid sequences encoding PANEC-1 and PANEC-2 at page 8, lines 14-18 and page 9, lines 10-20.

Therefore, Applicants submit that the present specification does indeed enable the practice of the claimed diagnostic tests without the need for undue experimentation. As noted by the CAFC in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir.), enablement is not precluded by the necessity for some experimentation:

> ". . . A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."

As is stated by the Examiner at page 6 of the outstanding Office Action the prior art enables methods of performing hybridization assays using known nucleic acid sequence. Applicants submit that the present application, in combination with the knowledge that was available in the art as of the filing date of this application, provides sufficient guidance to those of skill in the art as to how to practice the presently claimed invention without the need for undue experimentation; and the Examiner has shown no evidence to the contrary. Therefore, Applicants submit that new Claims 27-32 fully comply with the requirements of Section 112, first paragraph, and further submit that the teachings of the specification in combination with the knowledge of those of skill in the art at the time of filing of the present invention enable one to practice the claimed invention without undue experimentation.

Therefore, in view of the above arguments, Applicants respectfully request withdrawal of the Section 112, first paragraph, objection to the specification and rejection of claims.

V. Claims 1, 5, 6, 13, 17 and 18 Are Enabled

The Examiner has rejected Claim 1, 5, 6, 13, 17 and 18 under Section 112, 1st paragraph, stating that the disclosure is enabling only for claims limited to recombinant DNA molecules of defined sequence composition. The Examiner at page 10 of the present office action states that it is not clear what role PANEC-1 and 2 play in the complex genetic pathway of chemokines and therefore, it is not clear to the Examiner what role "variants" of PANEC 1 and 2 would play.

Applicants respectfully traverse this Section 112, 1st paragraph rejection of Claims 1, 5, 6, 13, 17 and 18 and assert that Claims 1, 5, 6, 13, 17 and 18, as amended, fully comply with Section 112, first paragraph requirements.

Preliminarily, Applicants submit that the genetic pathway of PANEC 1 and 2 does not need to be elucidated in order for the presently claimed invention to be enabled. Applicants have characterized PANEC-1 and -2 as C-C chemokines, which are known by those of skill in the art to be associated with inflammation, and have provided an amino acid alignment with related chemokines as support. This characterization, as illustrated in the present application, provides the basis for the presently claimed invention.

The Examiner accurately states that the specification enables the sequences of panec-1 and panec-2 cDNA. The Examiner states that the term "comprising" as recited in the claims is inclusive of any fragment or

derivative of a nucleic acid which possesses the sole criteria that it includes the nucleic acid sequence shown in SEQ ID NO:1 and SEQ ID NO:3.

Applicants submit that independent Claims 1 and 13 as amended, which recite an isolated polynucleotide comprising a nucleic acid encoding the polypeptide having the sequence as shown in SEQ ID NO:2 and SEQ ID NO:4, would include and encompass nucleic acid having those sequences, including for example, cloning or expression vectors or a specific, isolated genomic sequence containing the claimed polynucleotides. Applicants submit that the novel, claimed polynucleotides having the nucleic acid sequence as shown in SEQ ID NO:1 and 3, and the novel polypeptides they encode, having the amino acid sequence as shown in SEQ ID NO:2 and 4, are fully described throughout the specification and claims.

The Examiner states that the specification defines nucleic acid of SEQ ID NO:1 and SEQ ID NO:3 as encompassing variants encoding the same or similar polypeptides, and active fragments and questions the enablement of variants and fragments. Applicants submit that, while the presently claimed invention is directed toward specific polynucleotides, the specification also enables polypeptide and polynucleotide variants and active fragments. The present specification at page 6, lines 14-16, defines "PANECs" as polypeptides or active fragments thereof, which are encoded by mRNAs transcribed from the cDNAs of SEQ ID NO:1 and SEQ ID NO:3. The present specification discloses at page 6, lines 29-32, that recombinant variant polypeptides having amino acid insertions, deletions and substitutions may be created using recombinant DNA techniques and describes a chemotaxis assay for measurement of chemokine activity. The specification, at page 13, lines 1-5, discloses that peptide fragments which are immunogenic but not necessarily biologically active may be

used in the production of antibodies. Therefore, the specification teaches and enables immunogenically active fragments of the PANEC sequences disclosed herein. Also, there is basis in the specification, in the hydrophobicity plots (Figures 4 and 5) taken together with the amino acid sequences, for the mature chemokine sequences which are active fragments of the amino acid seqeunces disclosed in SEQ ID NO:2 and 4. Regarding polynucleotide variants, the specification, at page 8, lines 19-20 discloses that recombinant nucleic acid variants encoding PANEC-1 and PANEC-2, or similar polypeptides, may be prepared by making use of the redundancy of the genetic code.

Applicants submit that the claims must be read in view of the teachings of the specification as it would be interpreted by one possessing ordinary skill in pertinent art and that one of skill in the art would understand that, due to the degeneracy of the genetic code, numerous, specific nucleic acid sequences could encode the amino acid sequences disclosed in SEQ ID NO:2 and 4. Furthermore, it would be understood by those of skill in the art, that polynucleotides could be genetically engineered to encode specific variants of PANEC sequences; however, the presently claimed invention recites those specific polynucleotides encoding the polypeptides as shown in SEQ ID NO: 2 and 4. Applicants submit that the present specification enables all such polynucleotides that encode PANEC-1 and PANEC-2.

The Examiner states that the language of the claims as originally filed encompasses a genomic clone and that the specification does not teach the genomic structure of panec-1 and 2. The Examiner cites the decision in Amgen Inc. v. Chugai Pharmaceutical Co Ltd (18 USPQ2d, Nos 90-1273 1991, CAFC).

Preliminarily, Applicants contend that while specific, isolated genomic sequences might fall with in the scope of amended independent Claims 1 and 13,

it is not necessary to fully describe the genomic structure of panec-1 and 2 in order to enable the presently claimed invention which recites an isolated polynucleotide having a nucleic acid sequence encoding a PANEC molecule. Similarly, although an expression vector containing a polynucleotide of Claim 1 might fall within the scope of amended Claims 1 and 13, it is not necessary to describe the expression vector in order to enable the presently claimed invention.

Furthermore, Applicants contend that in contrast to the problems encountered by Amgen in the '008 patent where it was disclosed that the invention embraced means for preparing "numerous" polypeptide analogs of EPO and claimed the DNA encoding sequences that produced any EPO-like product, Applicants presently claimed invention is directed to those specific, isolated nucleic acid sequences which encode the polypeptides having the sequence as shown in SEQ ID NO:2 and 4, which have been identified as novel C-C chemokines found expressed in the pancreas. Applicants assert that they have explicitly described PANEC-1 and PANEC-2 so as to distinguish them from other amino acids, see the present specification, SEQ ID NO: 2 and 4, and have explicitly described how to obtain the novel chemokines throughout the specification.

The Examiner cites Fiers v. Sugano (CAFC, 25 USPQ 2d, Nos 92-1170, 1993) stating that for a specification containing statements that claimed DNA sequence is part of the invention, a reference to a potential method for isolating the sequence does not satisfy the written description requirement of Section 112, since the specification does not describe the DNA itself. Applicants contend that the polynucleotides which encode PANEC-1 and PANEC-2 as recited in amended independent Claims 1 and 13, as well as the amino acid sequences for PANEC-1 and PANEC-2, are explicitly and fully described

throughout the present specification and, therefore, fully comply with the written description requirements of Section 112, even under Fiers v. Sugano.

As to the Examiner's statement that

"unspecified nucleic acids comprising the panec gene are unpredictable", Applicants contend that the most predictable event in nature is the genetic code which provides that numerous nucleic acid sequences may encode a given amino acid sequence. Applicants submit that the amino acid sequences for PANEC-1 and -2 are explicitly described in the present application and therefore, any nucleic acid encoding them is described and enabled.

Furthermore, Applicants contend that it would not require undue experimentation to make or use the nucleic acids, expression vectors and host cells of the presently claimed invention. As illuminated by Wands supra, the fact that some experimentation may be required to practice the claimed invention does not support a finding of undue experimentation in this case.

In view of the above arguments and evidence, Applicants respectfully request that the Section 112, first paragraph rejection of Claims 1, 5, 6, 13, 17 and 18 be withdrawn.

VI. Claims 1, 5, 6, 13, 17 and 18 are Novel

The Examiner has rejected Claims 1, 5, 6, 13, 17 and 18 under 35 U.S.C. § 102(b) as being anticipated by Caput et al. (EP 0488900-A).

Applicants respectfully traverse this Section 102 rejection of claims.

As stated by the Court of Customs and Patent Appeals ("CCPA") in In re Marshall, 198 USPQ 344, 346 (CCPA 1978):

> "Rejections under 35 USC §102 are proper only when the claimed subject matter is identically disclosed or described in the prior "art. (emphasis added).

As stated by the Court of Appeals for the Federal Circuit ("CAFC") in Scripps Clinic & Research Fdn. V.Genentech, Inc. 927 F.2d 565, 1576, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991):

> "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of art." (emphasis added)

A single prior art reference must meet each and every claim limitation in order to constitute as anticipation under §102.

Applicants submit that applying this standard to the present case, it is clear that Caput et al does not anticipate the present invention.

As shown in the GenBank printout, the sequences disclosed in Caput do not have 100% identity to the sequences for PANEC-1 or PANEC-2. Therefore, as a matter of fact and law, the Section 102 rejection of Claims 1, 5, 6, 13, 17 and 18 over Caput et al. must fail. Furthermore, pursuant to the Examiner's suggestion, Applicants have amended the rejected Claims to recite the nucleotide sequences encoding PANEC-1 and PANEC-1.

Applicants submit that in view of the above arguments and evidence of record, the Section 102 rejection of claims is erroneous and respectfully request its withdrawal.

CONCLUSION

In view of the amendments to claims and the arguments and evidence or record, Applicants respectfully request that the Examiner withdraw the outstanding objections and rejection in this case. An early allowance of the

claims is respectfully requested.

Respectfully submitted,

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Date: April 29, 1996

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